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Preliminary Amendment

Applicant(s): Serial No.:

Morrison et al. 10/523,315

Filed:

For:

I August 2003

PHOTOACTIVATED ANTI-VIRAL AND ANTI-CANCER AGENT

## Amendments to the Claims

This listing of claims replaces all prior versions, and listings, of claims in the aboveidentified application:

## **Listing of Claims**

1. (original) A compound having formula I

$$R_3$$
 $R_2$ 
 $R_1$ 
 $R_2$ 
 $R_1$ 
 $R_2$ 
 $R_3$ 
 $R_4$ 
 $R_3$ 
 $R_4$ 
 $R_5$ 
 $R_7$ 
 $R_7$ 
 $R_7$ 
 $R_7$ 
 $R_7$ 
 $R_7$ 
 $R_7$ 
 $R_7$ 
 $R_7$ 
 $R_7$ 

wherein R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are each independently selected from the group consisting of an alkyl group, an alkenyl group, an alkynyl group, a nitrile, an azide, an aryl group, an aralkyl group, a heteroaryl group, a hydroxy group, an alkoxy group, an aryloxy group, an amine group, and a hydrogen atom, or any two of R1, R2 and R3 together form an aryl or heteroaryl ring; and wherein X is a counterion, with the proviso that where  $R_1 = R_3 = H$ ,  $R_2$  is neither methyl nor phenyl.

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2. (original) A compound having the formula II

$$R_3$$
  $R_2$   $R_1$   $R_2$   $R_1$   $R_2$   $R_1$   $R_2$   $R_3$   $R_4$   $R_4$   $R_5$   $R_6$   $R_7$   $R_8$   $R_8$ 

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wherein  $R_1$ ,  $R_2$  and  $R_3$  are each independently selected from the group consisting of an alkyl group, an alkenyl group, an alkynyl group, a nitrile, an azide, an aryl group, an aralkyl group, a heteroaryl group, a hydroxy group, an alkoxy group, an aryloxy group, an amine group, and a hydrogen atom, or any two of  $R_1$ ,  $R_2$  and  $R_3$  together form an aryl or heteroaryl ring, and wherein X is a counterion.

- 3. (original) The compound of claim 1 or 2 wherein  $R_1 = R_2 = H$  and  $R_3 = (C1-C4)$  alkyl.
- 4. (original) The compound of claim 1 wherein  $R_1 = R_2 = H$  and  $R_3 = CH_3$  (cis-dichlorobis(5,6-dimethyl-1,10-phenanthroline)rhodium (III) chloride; 56TMBP).
- 5. (original) The compound of claim 1 or 2 wherein  $R_1 = R_2 = (C1-C4)$  alkyl and  $R_3 = H$ .

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- 6. (original) The compound of claim 1 wherein  $R_1 = R_2 = CH_3$  and  $R_3 = H$  (cisdishlorobis(3,4,7,8-tetramethyl-1,10-phenanthroline)rhodium(III)chloride; OCTBP)
- 7. (original) The compound of claim 1 or 2 wherein  $R_1 = R_3 = H$  and  $R_2 = N-(C1-C4)$ alkyl.
- 8. (original) The compound of claim 1 wherein  $R_1 = R_3 = H$  and  $R_2 = N(CH_3)_2$  (cisdichlorobis {N,N-dimethylamino)-1,10-phenanthroline} rhodium(III)chloride; BISNMe2).
- 9. (original) The compound of claim 1 or 2 wherein  $R_1 = R_3 = H$  and  $R_2 = O-(C1-C4)$  alkyl.
- 10. (original) The compound of claim 1 wherein  $R_1 = R_3 = H$  and  $R_2 = O-CH_3$  (cisdichlorobis(3,7-dimethoxy-1,10-phenanthroline)rhodium(III)chloride; TMOBP).
- 11. (original) The compound of claim 1 wherein  $R_1 = R_3 = H$  and  $R_2 = O-(CH_2)(CH_3)_2$  (cis-dichlorobis(3,7-diisopropoxy-1,10-phenanthroline)rhodium(III)chloride; TIOBP).
- 12. (original) The compound of claim 1 or 2 wherein  $R_1 = R_3 = H$  and  $R_2 = (C1-C4)$  phenyl.
- 13. (original) Cis-dichloro {2,3-di(2-pyridyl)quinoxaline} {1,10 phenanthroline} rhodium (III) chloride (TAPPHEN).
- (original) Cis-dichlorobis (2,3-di(2-pyridyl)quinoxaline) rhodium (III) chloride (BISTAP).
- 15. (original) Cis-dichloro(dipyrido[3,2a-2'3'c]phenazine)(1,10-phenantroline) rhodium (III) chloride (DPPZPHEN).

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16. (original) Cis-dichlorobis {dipyrido(3,2-a: 2',3'-c)phenazine}rhodium (III) chloride (BISDPPZ).

17. (original) A method for reducing the level of pathogenic contaminants in a biological material comprising:

(a) contacting the biological material with an effective amount of at least one bisbipyridyl rhodium (III) compound having the formula I, II, III or IV:

$$R_3$$
 $R_2$ 
 $R_1$ 
 $R_1$ 
 $R_1$ 
 $R_2$ 
 $R_3$ 
 $R_2$ 
 $R_1$ 
 $R_1$ 
 $R_2$ 
 $R_3$ 
 $R_2$ 
 $R_1$ 
 $R_1$ 
 $R_2$ 
 $R_3$ 
 $R_2$ 
 $R_1$ 

wherein  $R_1$ ,  $R_2$  and  $R_3$  are each independently selected from the group consisting of an alkyl group, an alkenyl group, an alkynyl group, a nitrile, an azide, an aryl group, an aralkyl group, a heteroaryl group, a hydroxy group, an alkoxy group, an aryloxy group, an amine group, and a hydrogen atom, or any two of  $R_1$ ,  $R_2$  and  $R_3$  together form an aryl or heteroaryl ring; and wherein

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X is a counterion, with the proviso that where  $R_1 = R_3 = H$ ,  $R_2$  is not methyl, and where  $R_1 = R_2 = H$ ,  $R_3$  is not methyl;

$$R_3$$
  $R_2$   $R_1$   $R_2$   $R_1$   $R_2$   $R_3$   $R_4$   $R_5$   $R_6$   $R_7$   $R_8$   $R_8$   $R_9$   $R_9$ 

wherein  $R_1$ ,  $R_2$  and  $R_3$  are each independently selected from the group consisting of an alkyl group, an alkenyl group, an alkynyl group, a nitrile, an azide, an aryl group, an aralkyl group, a heteroaryl group, a hydroxy group, an alkoxy group, an aryloxy group, an amine group, and a hydrogen atom, or any two of  $R_1$ ,  $R_2$  and  $R_3$  together form an aryl or heteroaryl ring, and wherein X is a counterion;

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wherein R<sub>4</sub> and R<sub>4</sub>' together form a phen ligand, yielding *cis*-dichloro{2,3-di(2-pyridyl)quinoxaline}{I,10-phenanthroline}rhodium (III)chloride (TAPPHEN) or a "tap" ligand, yielding *cis*-dichlorobis{2,3-di(2-pyridyl)quinoxaline} rhodium (III) chloride (BISTAP);

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wherein R<sub>4</sub> and R<sub>4</sub>' together form a phen ligand, yielding cis-dichloro(dipyrido[3,2a-2'3'c]phenazine)(1,10-phenantroline) rhodium(III) chloride (DPPZPHEN) or a dppz ligand, yielding cis-dichlorobis{dipyrido(3,2-a: 2',3'-c)phenazine}rhodium (III) chloride (BISDPPZ);and

- (b) irradiating said biological material for a time sufficient to activate the bisbipyridyl rhodium (III) compound thereby causing a reduction the level of said pathogenic contaminants in said biological material.
- 18. (original) The method of claim 17 wherein the biological material comprises blood, semen, ascites fluid, milk, lymphatic fluid, an organ, a tissue, a hybridoma cell line, or components thereof.
- 19. (original) The method of claim 17 wherein the biological material comprises blood or blood components.
- 20. (original) The method of claim 19 wherein the biological material is substantially free of hemoglobin.
- 21. (original) The method of claim 20 wherein the biological material comprises at least one blood component selected from the group consisting of platelets, concentrated platelets, plasma, serum and blood proteins.
- 22. (original) The method of claim 17 wherein the biological material comprise diseased cells in a patient.
- 23. (original) The method of claim 22 wherein the diseased cells are tumor cells.

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- 24. (original) The method of claim 17 further comprising removing the biological material from patient prior to contacting the biological material with the bisbipyridyl rhodium (III) compound.
- 25. (original) The method of claim 24 wherein the biological material comprises blood, blood components, or tumor cells.
- 26. (original) The method of claim 24 further comprising returning the biological material to the patent after irradiation.
- 27. (currently amended) The method of claim [7] 17 wherein the biological material comprises tumor cells, the method further comprising returning the tumor cells to the patient prior to irradiation.
- 28. (original) The method of claim 17 wherein step (b) comprises irradiating the biological material with light having a wavelength of 310 nm to 400 nm.
- 29. (original) The method of claim 28 wherein the irradiating light has a wavelength of 320 nm to 400 nm.
- 30. (original) The method of claim 17 wherein step (b) comprises irradiating the biological material with light having a wavelength of > 400 nm.
- 31. (original) The method of claim 17 wherein the pathogenic contaminant comprises a pathogenic organism selected from the group consisting of a bacterium, virus and protozoan.

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- 32. (original) The method of claim 17 wherein the pathogenic contaminant comprises a leukocyte.
- 33. (original) The method of claim 17 wherein the pathogenic contaminant comprises a tumor cell.
- 34. (currently amended) The method of claim [1] 17 further comprising, after step (b), removing the bisbipyridyl rhodium (lll) compound from the biological material.
- 35. (original) The method of claim 17 further comprising, prior to step (b), contacting the biological material with a sensitizer molecule having an absorption maximum of greater than 550 nm; wherein step (b) comprises irradiating the biological material with light having a wavelength of greater than 550 nm so as to excite the sensitizer molecule and thereby indirectly activate the bisbipyridyl rhodium (III) compound.
- 36. (original) The method of claim 35 wherein the biological material comprises blood or blood components.
- 37. (original) The method of claim 35 wherein the biological material comprises red blood cells.
- 38. (original) The method of claim 35 wherein the biological material comprises hemoglobin.
- 39. (original) The method of claim 35 wherein the irradiation sensitizer molecule comprises methylene blue or a derivative thereof.
- 40. (original) The method of claim 35 wherein irradiation sensitizer molecule comprises acriding orange or a derivative thereof.

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41. (original) The method of claim 17 or 35 wherein the bisbipyridyl rhodium (III) compound is selected from the group consisting of *cis*-dichloro(dipyrido[3,2a-2'3'c]phenazine)(1,10-phenantroline) rhodium(III) chloride (DPPZPHEN), *cis*-dichlorobis(3,4,7,8-tetramethyl-1,10-phenanthroline) rhodium(III) chloride (OCTMP), *cis*-dichlorobis{dipyrido(3,2-a: 2',3'-c)phenazine}rhodium (III) chloride (BISDPPZ), *cis*-dichlorobis(3,7-dimethoxy-1,10-phenanthroline) rhodium(III) chloride (TMOBP), *cis*-dichlorobis(3,7-diisopropoxy-1,10-phenanthroline) rhodium(III) chloride (TIOBP), *cis*-dichlorobis{3,7(N,N-dimethylamino)-1,10-phenanthroline} rhodium(III) chloride (BISNMe2), *cis*-dichlorobis(4,7-diphenyl-1,10-phenanthroline) rhodium(III) chloride (TPBP), and *cis*-dichlorobis{2,3-di(2-pyridyl)quinoxaline} rhodium (III) chloride (BISTAP).

42. (original) The method of claim 17 or 35 wherein the bisbipyridyl rhodium (III) compound is DPPZPHEN, OCTMP or BISNMe2